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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,812	07/10/2001	Diane Pennica	GENENT.083A	7879

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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/901,812	PENNICA ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,8-10,67-69,71-76 and 78-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,8-10,67-69,71-76 and 78-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20050317; 20041022*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 17, 2005 has been entered.

1. The amendment filed March 17, 2005 is acknowledged and has been entered. Claims 5, 70, and 77 have been canceled. Claims 1, 3, 4, 67-69, and 74-76 have been amended.

2. Claims 1, 3, 4, 8-10, 67-69, 71-76, and 78-80 are pending in the application and currently under prosecution.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

4. The information disclosure filed October 20, 2004 has been considered. An initialed copy is enclosed.

Declaration

5. Receipt of the new declaration filed March 17, 2005 is acknowledged.

Grounds of Objection and Rejection Withdrawn

6. Unless specifically reiterated below, Applicant's amendment and/or arguments submitted March 17, 2005 have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed October 20, 2004.

Grounds of Rejection Maintained

Claim Rejections – 35 USC § 112

7. The rejection of claims 1, 3, 4, 8-10, 67-69, 71-76, and 78-80 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is maintained.

The initial ground of rejection is set forth in section 7 of the preceding Office action mailed October 20, 2004; however, Applicant is advised that additional considerations have been made in light of Applicant's amendment filed March 17, 2005, which require Applicant's attention.

At pages 8-10 of the amendment filed March 17, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, "Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

The claims are drawn to a method comprising treating tumors cells characterized by aberrant Wnt signaling for the purpose of selectively enhancing the expression of a Stra6 protein in the tumor cells.

In order to use the claimed invention, one necessarily has to have a tumor cell characterized by aberrant Wnt signaling. As noted in the preceding Office actions, the specification defines the term "characterized by aberrant Wnt signaling" as including "genetic defects and/or altered expression patterns (including mutations, amplification, over-expression and/or suppression) of any of these members of the Wnt signaling pathway, or any other members, known today **or hereinafter identified**" (emphasis added) (lines 9-11). Accordingly, the claims are directed to a member of a genus of tumor cells that are characterized as having genetic defects and/or altered expression patterns, including mutations, amplification, over-expression, and/or suppression of any member of a genus of known, *or yet to be discovered* proteins involved in a Wnt signaling pathway.

As explained in the preceding Office actions, the disclosed or known members of the Wnt signaling pathway are disparate in structure and function. Accordingly, it is submitted that the skilled artisan could not immediately envision, recognize, or distinguish the tumor cells that must be possessed to practice the claimed invention, since, for example, the skilled artisan cannot hope to predict the structure of any hereinafter identified members of a Wnt signaling pathway.

The Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568). Certainly, in this instance, because the specification specifically directs the artisan to the use of tumor cells harboring defects causing aberrant expression of any hereinafter identified members of a Wnt signaling pathway, it cannot be reasonably said that having described a few known members of such a pathway, the supporting disclosure of the claimed invention satisfies the written description requirement.

Furthermore, "generalized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004). In this instance, there is no language that adequately describes at least a substantial number of the members of the genus of proteins involved in a Wnt signaling pathway that are aberrantly expressed in tumor cells that may be treated with an effective amount of a retinoid to achieve the claimed effect. A description of what a material does, or how it is expressed, rather than of what it is, does not suffice to describe the claimed invention. If the skilled artisan could not immediately envision, recognize or distinguish the members of the genus of aberrantly expressed proteins involved in Wnt signaling, then, the skilled artisan could not immediately recognize or distinguish the tumor cells that must be used in practicing the claimed invention.

"Regardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to the subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods". *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1894 (CAFC 2004). The claimed method depends upon finding tumor cells that are characterized by aberrant Wnt signaling, which when treated with a retinoid, selectively express a Stra6 protein at enhanced levels; without such tumor cells, it is impossible to practice the invention.

Although the skilled artisan could potentially identify such tumor cells that might be used in practicing the claimed invention by performing experiments that are designed to identify members of a Wnt signaling pathway and detect tumor cells having defects or abnormalities in a Wnt signaling pathway that result from mutations affecting the expression or activity of those members, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

Finally, Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description" Requirement (66 FR 1099-1111, January 5, 2001) states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims are directed to a genus of RNA molecules, which vary both structurally and functionally, despite being commonly over-expressed in colorectal cancer, relative to normal colorectal tissue, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. In this instance, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; Applicant has not shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; and Applicant has not described distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention at the time the application was filed.

The claims have been amended to recite, "for the enhancement of the expression of **a Stra6 protein**" (emphasis added), whereas claim 5 (now canceled),

which had been considered in the prior Office actions, limited the protein of claim 1 to Stra6, as opposed to "a Stra6 protein". While Stra6 is a known protein, the claims are now more broadly directed to a genus of "Stra6" proteins, including but not limited to Stra6. At page 8, lines 9-13, for example, the specification describes this genus of proteins as including Stra6 and structurally disparate variants, which may or may not retain or share the function of Stra6. Accordingly, the claims are directed to a method for selecting enhancing the expression of a member of a genus of structurally and functionally variant proteins in a tumor cell. The claims do not limit the proteins to any particular degree, either in terms of structure or function. While the prior art adequately describes Stra6, it does not necessarily adequately describe the structural and functional variants of Stra6 to which the claims are directed. Moreover, in light of the degree of structural and functional differences permitted by the claims, it would not be understood how, or why it would be reasonably asserted that Stra6 is representative of the genus of proteins, as a whole. Given the lack of adequate description of the genus, which might permit the skilled artisan to instantly envision, recognize, or distinguish the members of the genus of "Stra6 proteins" to which the claims are directed, the supporting disclosure would not reasonably convey to the artisan that Applicant had possession of the claimed invention at the time the application was filed.

Applicant has argued that given the present knowledge in the art regarding the Wnt signaling pathway, the instant description of multiple species of tumors cells characterized by aberrant Wnt signaling would reasonably convey that Applicant had possession of the claimed invention at the time the application was filed. However, as noted previously, since the members of the genus are so variant in structure and function, the instant description of some species of tumor cells characterized by aberrant Wnt signaling cannot suffice to describe the genus as a whole, because, even given benefit of the instant disclosure of the claimed invention, the skilled artisan could not instantly envision, recognize, or distinguish at least a substantial number of the members of the genus. The examples described are not representative of the genus as a whole, since, for example, the genus includes members characterized by defects or

abnormal levels of expression of signaling molecules, which have yet to be discovered, isolated, or described.

Furthermore, apart from the tumor cells described in the specification as having aberrant Wnt signaling, the skilled artisan cannot envision or predict the nature of the genetic defects and/or altered expression patterns, including mutations, amplification, over-expression, and/or suppression of the known members of the Wnt signaling pathway, so as to immediately recognize any other tumor cells having aberrant Wnt signaling.

Beginning at page 8, Applicant has argued that the supporting disclosure adequately describes the tumor cells characterized by aberrant Wnt signaling, since, for example, at pages 13-14, the specification provides some description of Wnt signaling pathways and the factors that are known to be involved in such pathways. Pointedly, however, the claims are not limited to those members of a Wnt signaling pathway that are adequately described by the supporting disclosure, but are instead directed to a much broader genus of proteins, which includes members that have not yet been identified. Moreover, the specification describes members of the genus as, for example, the "Frizzled-Receptor-Like Proteins"; but while one might recognize the known and/or prototypal members of this family of proteins, the supporting disclosure fails to describe what common structures and functions characterize the its members collectively. Furthermore, many proteins have structurally and functionally different isoforms, which are produced, for example, by alternative splicing; so, in some instances, even if the prototypal member of a family of proteins (e.g., Frizzled) is known, the use of the name given the prototypal member may not serve to identify a single protein, but rather may identify a genus of proteins that are structurally and functional variant.

At page 9, Applicant has argued that given the description of the members of Wnt signaling pathways provided and the further description of multiple examples of tumor cells or tissues that have been found to have altered expression of such members, the specification would permit the skilled artisan to recognize the tumor cells necessary to use the claimed invention. Again, it is submitted that the members of Wnt signaling pathways that are adequately described in the specification are not

representative of the members that have not been described, as the skilled artisan could not immediately envision, recognize or distinguish such other members of the genus; therefore, the skilled artisan could not immediately envision, recognize or distinguish at least a substantial number of the tumor cells to which the claims are directed. Furthermore, given the breadth of the claims, or more particularly the size and variability of the genus of proteins involved in a Wnt signaling pathway, the examples of tumor cells that are provided in the specification cannot be reasonably be considered representative of the genus of tumor cells characterized by aberrant Wnt signaling.

Applicant has argued the fact that some members of the Wnt pathway have not yet been described does not negate the detailed description of many of the members of the pathway. Again, the claims are not limited to cells characterized by defects associated with mutations to those members of a Wnt signaling pathway that are adequately described.

Applicant has argued that the description of those members, which Applicant asserts is adequate, would readily allow the skilled artisan to recognize other members of the pathway, as such a molecule is *likely* to interact with known members of the pathway. If, such a molecule is only likely to interact with known members of the pathways, how does one recognize members of a Wnt signaling pathway that do not interact with known members? Even if the other members interact with known members, how does one recognize tumor cells characterized by aberrant Wnt signaling by distinguishing proteins that bind known members of the pathways from others?

At page 10, Applicant has remarked, "Applicants do not need to describe the structure and function of each member of the pathway, but only that it is a member of the pathway" (paragraph 1). In response, the claims are directed to tumors cells characterized as having defects in the expression or activity of members of a Wnt signaling pathway that have not yet been identified.

Applicant has asserted, "[m]embers of the pathway are identified by their relationship to one another" (page 10, paragraph 1). If members are not yet identified, how does one recognize a relationship between such unidentified members and other

members? Furthermore, what "relationship" between two members of the pathway is it that identifies members of the pathway?

Applicant has remarked that the Examiner has not cited evidence that all of the described genes are not members of the Wnt signaling pathway. In reply, it is not the position of the Office that members of the pathway that have been described are not members of the pathway.

Claim Rejections - 35 USC § 102

8. The rejection of claims 1, 3, 4, 8-10, 67-69, 71-76, and 78-80 under 35 U.S.C. 102(a) as being anticipated by Chu et al. (of record), as evidenced by Pennica et al. (of record) and Szeto et al. (of record), is maintained.

At pages 11-13 of the amendment filed March 17, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

The claims are drawn to a method comprising treating tumors cells characterized by aberrant Wnt signaling for the purpose of selectively enhancing the expression of a Stra6 protein in the tumor cells.

The prior art teaches treating tumor cells with a retinoid, namely retinoic acid.

The prior art does not expressly teach that the tumor cells treated with the retinoid are characterized by aberrant Wnt signaling. Nevertheless, as evidenced by Pennica et al., the colon cancer cells (i.e., HT-29 cells) of the prior, which were treated with retinoic acid, are characterized by aberrant Wnt signaling, since Pennica et al. discloses the gene encoding WISP-1 is amplified in those cells (page 14720, column 2).

While the prior art does not teach that the expression of a Stra6 protein in the tumor cells treated with the retinoid has been selectively enhanced, the claims do not recite that such selective enhancement is necessarily achieved. Moreover, the recitation, "for the selective enhancement of the expression of a Stra6 protein in a tumor cell" is regarded as merely the intended purpose of performing the process that Applicant regards as the invention. The recitation does not limit, materially or

structurally, any one element used in practicing the claimed process, nor does it necessarily limit the mechanical operation that process. Even so, because the prior art teaches treating the tumor cells with retinoic acid induces gene expression in those cells, the process of the prior art is deemed capable of selectively enhancing the expression of any gene in the cells that is inducible upon treatment of the cells with a retinoid. As evidenced by Szeto et al., the gene encoding Stra6 is retinoic acid-responsive; and therefore, it is reasonably expected that the process disclosed by the prior art did in effect cause the selective enhancement of expression of a Stra6 protein in the tumor cells treated with the retinoid. The Office, however, does not have the facilities for examining and comparing Applicant's process with the process of the prior art. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed process and the process taught by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

At page 12, Applicant has remarked that the prior art does not disclose selective enhancement of Stra6 proteins in a tumor cell characterized by aberrant Wnt signaling. In reply, it cannot be understood how the process claimed differs from the process disclosed by the prior art. The process claimed comprise the step of treating tumor cells with an effective amount of a retinoid to selectively enhance the expression of a Stra6 protein in the tumor cells. It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See *Bristol-Myers Squibb Company v. Ben Venue Laboratories*, 58 USPQ2d 1508 (CAFC 2001).

Moreover, the specification does not distinguish an amount of retinoid that is effective to selectively enhance expression of a Stra6 protein from the amount of retinoid that was used to treat the tumor cells in the process described by the prior art. Because the prior art discloses an induction of gene expression occurred upon treatment of the cells with the amount of retinoid disclosed, absent a showing of any difference, the amount disclosed is reasonably deemed an amount effective to

selectively enhance the expression of any gene, including the gene encoding Stra6 that is inducible upon the treatment of such cells with the retinoid.

Applicant has argued that the prior art fails to anticipate the claimed invention because the prior art does not disclose "the synergistic enhancement of expression by a combination of Wnt pathway and said retinoid" (page 12, paragraph 2). In reply, claim 67 recites, "wherein said Stra6 protein is characterized by synergistic enhancement of its expression by a combination of Wnt-1 and said retinoid". Notably, none of the claims recite that, as Applicant has asserted the prior art fails to teach, the claimed process results in "the synergistic enhancement of expression by a combination of Wnt pathway and said retinoid". Even so, presuming that it was Applicant's intention to assert that the prior art does not disclose that the process results in the selective enhancement of expression of a Stra6 protein, which is characterized by synergistic enhancement of its expression by a combination of Wnt-1 and said retinoid, then, it is again noted that the claimed process does not necessarily have to cause the selective enhancement of expression of a Stra6 protein, since the recitation is only considered the intended use for the claimed process. Furthermore, if the process results in the selective expression of Stra6, as opposed to any other "Stra6 protein", as evidenced by Szeto et al., it is aptly noted that the expression of the gene encoding Stra6 is, in fact, synergistically enhanced by retinoic acid in the presence of enforced expression of a gene encoding Wnt-1. Again, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

At page 12 of the amendment, Applicant has argued that the prior art does not teach that the amount of retinoic acid used to treat the tumor cells is an effective amount to selectively enhance the expression of genes in those cells that are inducible upon treatment of the cells with the retinoid. To support this argument, Applicant has remarked, the prior art "explicitly states that the induction of Gpx2 mRNA in MDA MB-231 and HT-29 was not significant" (page 12, paragraph 3). Chu et al. discloses that the amount of retinoic acid used to treat the cells caused a 12-fold induction in the expression of the gene encoding Gpx2 in MCF-7 cells (page 1849, column 2); therefore, contrary to Applicant's assertion, the amount of retinoic acid used to treat the tumor

cells is an effective amount to selectively enhance the expression of genes in those cells that are inducible upon treatment of the cells with the retinoid. Although at page 1851, column 1, as Applicant has remarked, Chu et al. teaches that the level of induction of the gene in MCF-7D1, MDA-MB-231, and HT-29 cells "was not significant", in Table 2 (page 1851), Chu et al. discloses that increases in the level of expression of the gene were observed in each of the cell lines, except for MDA-MB-231. Despite the significance, or lack thereof, of an increase of such a small magnitude, the prior art teaches a selective enhancement of expression in the tumor cells resulted from treatment of those cells with an amount of retinoic acid effective amount to selectively enhance the expression of genes in those cells that are inducible upon treatment of the cells with the retinoid. Furthermore, the claims do not require the enhancement of gene expression in the tumor cells treated to be "significant", or of any particular magnitude; and as explained, the claims do not require the selective enhancement of any particular gene, only that the amount of retinoic acid used to treat be an effective amount to selectively enhance the expression of a Stra6 protein in a tumor cell. Again, the specification does not distinguish an amount of retinoid that is effective to selectively enhance expression of a Stra6 protein from the amount of retinoid that was used to treat the tumor cells in the process described by the prior art. Chu et al. teaches an amount of retinoic acid effective to selectively enhance the expression of a gene in a tumor cell. The amount disclosed is reasonably deemed an amount effective to selectively enhance the expression of any gene, including a gene encoding a Stra6 protein that is inducible upon the treatment of such cells with the retinoid.

As in the response to the preceding Office action, Applicant has again addressed the propriety of citing references published after the filing date of the instant application as evidence. As explained before, it is proper to cite such references to establish inherent features.

MPEP § 2112 states:

> The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and

> obviousness." *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) (affirmed a 35 U.S.C. 103 rejection based in part on inherent disclosure in one of the references). See also *In re Grasselli*, 713 F.2d 731, 739, 218 USPQ 769, 775 (Fed. Cir. 1983).
>
> There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure *at the time of invention*, but only the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

MPEP § 2112 further states that the Examiner must provide rationale or evidence tending to show inherency:

> The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) [...]. "To establish inherency, the extrinsic evidence must make clear the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill [...] *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) [.]

Furthermore, MPEP 2131.01, which although specifically addressing the proper use of multiple references in 35 U.S.C. § 102 rejections, is worthy of note also, since it states:

> "To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such a gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that is would be so recognized by persons of ordinary skill." *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) [....] Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO, Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999) [....] [T]he critical date of extrinsic evidence showing a universal fact need not antedate the filing date. See MPEP § 2124.

MPEP § 2124 states the exception to the rule that the critical reference date must precede the filing date:

> In certain circumstances, references cited to show a universal fact need not be available as prior art before applicant's filing date. *In re Wilson*, 311 F.2d 266, 135 USPQ 442

> (CCPA 1962). Such facts include characteristics and properties of a material or a scientific truism.

Thus, the MPEP makes clear that the inherent teaching of the prior art is a question of fact that arises in both 102 and 103 rejections. While there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure *at the time of invention*, it is the Examiner's obligation to provide extrinsic evidence, which need not antedate the filing date of the application, showing the missing descriptive matter is necessarily present in the thing described in the reference, and that is would be so recognized by persons of ordinary skill.

In this instance, the claims are directed to a process comprising treating a tumor cell with an effective amount of a retinoid to selectively enhance the expression of a Stra6 protein in a tumor cell. While Chu et al. does not teach that the amount of retinoic acid that was used to treat the tumor cells is effective to selectively enhance the expression of a Stra6 protein in a tumor cell, the capability of that amount of retinoid to do so is an inherent characteristic of that quantity or concentration. Chu et al. provides factual evidence that the amount of retinoic acid used to treat the tumor cells is an amount that is effective to selectively enhance the expression of genes in those tumor cells that are inducible upon treatment of the cells by retinoic acid. While Chu et al. does not teach that the gene encoding Stra6 is so inducible, its ability to be induced by an effective amount of retinoic acid is an inherent property. Szeto et al. teaches that Stra6 is, in fact, a gene that is inducible by such treatment of cells. While Chu et al. does not teach that the tumor cells are characterized by aberrant Wnt signaling, such properties of the cells are inherent. Pennica et al. teaches that HT-29 cells are, in fact, characterized by aberrant Wnt signaling.

Thus, it is the Office's position that the express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. §§ 102 and/or 103. There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure *at the time of invention*, but only the subject matter is in fact inherent in the prior art reference; and references cited to show a universal fact need not be available as prior art before Applicant's filing date.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 3, 4, 8-10, 67-69, 71-76, and 78-80 are rejected under 35 U.S.C. 102(b) as being anticipated by van der Leede et al. (*Mol Carcinog.* 1993;8 (2): 112-122), as evidenced by Szeto et al. (of record).

The claims are drawn to a method comprising treating tumors cells characterized by aberrant Wnt signaling for the purpose of selectively enhancing the expression of a Stra6 protein in the tumor cells.

van der Leede et al. teaches treating colon carcinoma HTC116 cells with retinoic acid; see entire document (e.g., the abstract).

van der Leede et al. does not expressly teach that HTC116 cells are characterized by aberrant Wnt signaling, nor does van der Leede et al. teach that treating tumor cells with retinoic acid selectively induces the expression of Stra6 in those cells. Nevertheless, as evidenced by Szeto et al., HCT116 cells carry an activating mutation in the gene encoding β-catenin and treating HCT116 cells with retinoic acid induces the expression of the gene encoding Stra6 in those cells (page 4202, column 2).

11. Claims 1, 3, 4, 8-10, 67-69, 71-76, and 78-80 are rejected under 35 U.S.C. 102(b) as being anticipated by Keogh et al. (*Cancer Biochem Biophys.* 1993 Jun; **13** (3): 209-220), as evidenced by Szeto et al. (of record).

The claims are drawn to a method comprising treating tumors cells characterized by aberrant Wnt signaling for the purpose of selectively enhancing the expression of a Stra6 protein in the tumor cells.

Keogh et al. teaches treating colon carcinoma WiDr cells with retinoic acid; see entire document (e.g., the abstract).

Keogh et al. does not expressly teach that WiDr cells are characterized by aberrant Wnt signaling, nor does Keogh et al. teach that treating tumor cells with retinoic acid selectively induces the expression of Stra6 in those cells. Nevertheless, as evidenced by Szeto et al., WiDr cells have lost both copies of the gene encoding APC and treating WiDr cells with retinoic acid induces the expression of the gene encoding Stra6 in those cells (page 4202, column 2).

Conclusion

12. No claim is allowed.

13. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Yan et al. (*Proc. Natl. Acad. Sci. U S A.* 2001 Dec 18; **98** (26): 14973-8) teaches determinig whether the Wnt/b-catenin signaling pathway is activated in clinical cancer samples is not easy.

14. Applicant's request for an interview is acknowledged. Applicant is invited to telephone the Examiner to schedule a date and time for such an interview.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
May 27, 2005